REMARKS

The Office Action

Claims 16, 17, 24, 25, 27, 44-46, 48-50, 70-89 and 117-130 are pending in the application. All claims stand rejected under 35 U.S.C. § 112, second paragraph and under 35 U.S.C. § 103(a) as being obvious over Spence et al. (U.S. Publication 2002/0005354; hereafter "Spence") in view of Chou et al. (PNAS 96:11-13 (1999); hereafter "Chou").

Rejection under 35 U.S.C. § 112, second paragraph

All pending claims stand rejected under 35 U.S.C. § 112, second paragraph for failing to particularly point out and distinctly claim the subject matter of the invention.

Regarding definiteness, M.P.E.P. § 2173.02 states:

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity.

The Examiner's suggested claim language is carefully considered, but, based on the standard recited above, applicants respectfully decline to adopt the suggested amendment. Instead, applicants submit that a skilled artisan would understand the invention recited in claim 44 and each of its elements and limitations in light of the specification.

Instant claim 44, from which all other claims depend, recites:

> A method of producing a cell population enriched in a first type of cell larger than an adult, enucleated red blood cell, said method comprising the steps of subjecting a blood sample to (i) separation comprising contact

with a microfluidic device comprising obstacles separated by gaps, so that adult, enucleated red blood cells and cells smaller than adult, enucleated red blood cells are directed in one direction and cells larger than adult, enucleated red blood cells are directed in a second direction to produce a ***first sample enriched in said cells larger than adult, enucleated red blood cells***, and (ii) separation comprising contacting said first sample with a microfluidic device comprising obstacles that preferentially bind said first type of cell in said first sample, thereby producing a population enriched in said first cell type. (emphasis added).

As emphasized above, claim 44, step (i) results in a "first sample enriched in said cells ***larger than*** adult, enucleated red blood cells" **not** a first sample that is enriched in adult, enucleated red blood cells as suggested by the Examiner. Furthermore, the Examiner's suggested claim language would not be appropriate for the practice of one of the preferred embodiments of the invention, namely the enrichment of fetal, nucleated red blood cells. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejection under 35 U.S.C. § 103(a)

All pending claims stand rejected as being obvious over Spence in view of Chou. As noted by the Examiner, Spence teaches a method of enriching a first cell type in a microfluidic device, and Chou teaches the use of support pillars in the channels of a microfluidic device. The Examiner states that a person having ordinary skill in the art would have combined the teachings of Spence and Chou to practice the present invention.

As recited in M.P.E.P. § 2144.08:

> A proper obviousness analysis involves a three-step process. First, Office personnel should establish a *prima facie* case of unpatentability considering the factors set out by the Supreme Court in *Graham v. John Deere*. See, e.g., *In re Bell*, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993) ("The PTO bears the burden of establishing a case of *prima facie* obviousness."); *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966), requires that to make out a case of obviousness, one must:
>
> (A) determine the scope and contents of the prior art;
>
> (B) ascertain the differences between the prior art and the claims in issue;
>
> (C) determine the level of >ordinary< skill in the pertinent art; and
>
> (D) evaluate any evidence of secondary considerations.

The present rejection does not meet this standard.

Claim 44, recited above, requires two steps. Step (i) recites a size-based enrichment of a first type of cell that is larger than an adult, enucleated red blood cell by passing a blood sample through a microfluidic device that contains obstacles separated by gaps. Step (ii) recites a further enrichment of this first type of cell by requiring that the obstacles preferentially bind the first type of cell as it passes through the microfluidic device. Neither Spence nor Chou teach or support either of these steps. Accordingly, even if Spence or Chou were combined, this combination cannot teach or suggest the present invention.

In support of the arguments made above, applicants provide a declaration from inventor Dr. Kapur. Dr. Kapur holds a Ph.D. in bioengineering and has an extensive publication record in this field. In the declaration, Dr. Kapur identifies two aspects of the present invention that significantly differ from the teachings of Spence and Chou. First,

Dr. Kapur notes that neither Spence nor Chou teaches the separation of cells based on size using a microfluidic device comprising obstacles separated by gaps, but rather each teaches support pillars to prevent collapse of their respective microfluidic channels. As stated by Dr. Kapur, these pillars do not play a role in the cell sorting process:

> Neither Spence et al. nor Chou et al. teaches the separation of cells based on size using a microfluidic device comprising obstacles separated by gaps. The support pillars shown in Fig. 6 of Spence et al. and Fig. 1 of Chou et al. ***function only to prevent the microfluidic channel from collapsing***, i.e., they only serve to prevent the lid from caving into the microfluidic channel. In Spence et al., a cell is sorted as it passes through a detection region. The pillars in Fig. 6 of Spence are not located in the detection region and are not involved in the cell sorting process that occurs in the detection region. Chou et al. describes the sorting of DNA molecules and not cells. DNA molecules in Chou et al. are sorted at a T-junction that does not contain pillars, and the pillars are not involved in the sorting that occurs at the T-junction. Furthermore, as a result of passing through the pillars in the devices depicted in Fig. 6 of Spence et al. and Fig. 1 of Chou et al., adult, enucleated red blood cells and cells smaller than adult, enucleated red blood cells would not be directed in one direction, and cells larger than adult, enucleated red blood cells would not be directed in a second direction. (emphasis added)

Furthermore, Dr. Kapur notes that the present invention also requires the preferential binding of cells to obstacles in a microfluidic channel. This step is not taught or suggested by either prior art reference. Dr. Kapur states:

> Neither Spence et al. nor Chou et al. discloses preferential binding of cells to obstacles in a microfluidic channel. As described above, cells or molecules are separated as they pass through a detection region or T-junction. Furthermore, as stated above, the pillars present in Fig. 6 of Spence et al. and Fig. 1 of Chou et al. support the channel to prevent it from collapsing as cells and molecules flow through the channel to be sorted at the detection region or T-junction. In order to pass through the detection region or T-junction, the cells and molecules must not be bound to the channel or the pillars supporting it. Thus, the pillars described in Spence et

al. and Chou et al. ***are not designed to bind cells preferentially***. (emphasis added)

Thus, Spence and Chou fail to teach or suggest a microfluidic device containing obstacles that serve to enrich cells, as claimed in the present invention.

Applicants respectfully submit that the teachings of Spence and Chou, taken together, do not meet the standards of a *prima facie* case of obviousness as outlined in M.P.E.P. § 2144.08. In particular, the teachings of Spence and Chou are significantly different from the present invention and fail to provide each and every claim limitation. For the reasons outlined above, applicants request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested.

Applicants note that Forms PTO 1449 that were submitted with Information Disclosure Statements filed on April 16, 2007 and July 2, 2007 have not been initialed and returned, and hereby request that they be initialed and returned with the next Office action.

Enclosed is a Petition to extend the period for replying to the Office action for 3 months, to and including January 28, 2008, January 27, 2008 being a Sunday.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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